UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/640,041	08/15/2000	W. Michael Kavanaugh	1615.002/200130.503	2270

27476 7590 02/11/2004

Chiron Corporation
Intellectual Property - R440
P.O. Box 8097
Emeryville, CA 94662-8097

EXAMINER	
BELYAVSKYI, MICHAIL A	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 02/11/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/640,041	KAVANAUGH ET AL.	
	Examiner	Art Unit	
	Michail A Belyavskyi	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12/01/04*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-37* is/are pending in the application.

4a) Of the above claim(s) *10-13 and 15-37* is/are withdrawn from consideration.

5)☒ Claim(s) *2* is/are allowed.

6)☒ Claim(s) *1,3-9 and 14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

RESPONSE TO APPLICANT'S AMENDMENT

Applicant's amendment, 12/01/04 , is acknowledged.

Claims 1-37 are pending.

Claims 10-13 and 15-37 stand withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to a non-elected invention.

Claims 1-9 and 14 read on an isolated nucleic acid molecule wherein said isolated nucleic acid molecule comprising a polynucleotide which encodes SEQ ID NO: 4 and the nucleic molecule is SEQ ID NO: 3 are under consideration in the instant application.

In view of the amendment, filed 12/01/04 the following rejection remains:

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1, 3 -9 and 14 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for: 1) an isolated nucleic acid molecule comprising a polynucleotide selected from the group recited in claim 1 (a) – (c); 2) an isolated nucleic acid molecule comprising 345 contiguous nucleotides of SEQ ID NO:3, as recited in claim 2 ; a method of making a recombinant vector comprising inserting a nucleic acid molecule of claim 1 (a) –(c), and said recombinant vectors and a method of making a recombinant host cell comprising introducing said recombinant vectors, a recombinant host cell thereof and a method of producing a polypeptide comprising culturing said host cells as recited in claims 5-9 does not reasonably provide enablement for: A) *any* isolated nucleic acid molecule comprising a polynucleotide recited in claim 1 (d); B) *any* isolated nucleic acid molecule comprising a polynucleotide encoding a polypeptide having amino acid sequence from 1 to 115 of SEQ ID NO:4, or from about 2 to about 115 of SEQ ID NO:4, wherein said polypeptide has at least one conservative amino acid substitution and at least 90 % identity with SEQ ID NO:4 , as recited in claim 3; D) any composition comprising an isolated polynucleotide encoding a polypeptide comprising an amino acid sequence from 4 to 50 of SEQ ID NO: 4 or at least 90 % identical to a polypeptide comprising an amino acid sequence from 4 to 50 of SEQ ID NO:4 as recited in claim 14 for the same reasons set forth in the previous Office Action, mailed on 07/14/03

It is also noted that the terms "comprising" is an open-ended and expand isolated nucleic acid molecule comprising an amino acid sequence from 4 to 50 of SEQ ID NO:4 or at least 90 % identical to a polypeptide comprising an amino acid sequence from 4 to 50 of SEQ ID NO:4 as recited in claim 14, to include additional non disclosed amino acid sequences .

Applicant's arguments, filed 12/01/04 have been fully considered, but have not been found convincing.

Applicant asserts that : (i) the issue is not whether one skill in the art can predict whether a selected variant protein of EGFH2 will or will not nave the biological activity, but rather whether undue experimentation is required to test such variant for the activity; (ii) the specification provided a detailed method of screening for the biological activity of said variant protein of EGFH2 using *Xenopus* oocyte maturation assay and thus no undue experimentation is required.

Contrary to Applicant's assertions, the issue raised by the examiner was that the specification fails to provide sufficient guidance as to which core structure of SEQ ID NO: 4 is essential for maintain its mitogenic activity and which changes can be made in the structure of SEQ ID NO: 4 and still maintained the same function.

Applicant is relying upon certain biological activities and the disclosure of a single species to support an entire genus. The claims as written encompass a broad genus of polypeptides with an unlimited number of possibilities with regard to the length of the polypeptide sequence. Further, making changes up to 10% of a polynucleotide sequences does not provide that the encoded protein will retain the same mitogenic activity as the unmutated polynucleotide. The enablement issues of making said nucleic acid molecule encoding a polypeptide at lest 90 % identical to EGFH2 (SEQ ID NO:4) , having at least one specific conservative amino acid changes selected from the group recited in claims 1(d) and 14 (b) and having the same biological function is still remain because the specification does not teach and provide sufficient guidance as to which amino acid of SEQ ID NO:4 would have been altered such that the resultant polypeptide would have retained the same function, i.e. mitogenic activity as determined using *Xenopus* oocyte maturation assay. Therefore, absent the ability to predict which of these nucleic acid would encode peptides that would function as claimed, and given the lack of data on regions critical for activity, for one of skill in the art to practice the invention as claimed would require a level of experimentation that is excessive and undue.

A description of a protein by functional language, i.e ., having mitogenic activity as determined using *Xenopus* oocyte maturation assay in the absence of a structure is not considered sufficient to overcome 112 first rejection. See Fiers, 984 F.2d at 1169-71, 25 USPQ2D at 1605-06. It is only a definition of a useful result rather than a definition of what achieves that result. Many species may achieve that result. The definition requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736 /f.2d 1516, 1521, 22 USPQ 369, 372-73 (Fed. Cir. 1984) affirming the rejection because the specification does "little more than outline[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.") Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what the material consists of (e.g. structural feature), is not a description of that material.

Since the instant fact pattern fails to indicate that representative number of structurally related compounds is disclosed, the artisan would not know the identity of a reasonable number of representative compounds falling within the scope of the instant claims and consequently would not know how to make them. An assay for *finding or screening* a product, i.e. variant protein of EGFH2 that has mitogenic activity as determined using *Xenopus* oocyte maturation assay is not equivalent to a positive recitation of *how to make* a product.

It is well known that minor structural differences among even structurally related compounds or compositions can result in substantially different biology, expression, and pharmacology of proteins. Therefore, structurally unrelated A) *any* isolated nucleic acid molecule comprising a polynucleotide recited in claim 1 (d); B) *any* isolated nucleic acid molecule comprising a polynucleotide encoding a polypeptide having amino acid sequence from 1 to 115 of SEQ ID NO:4, or from about 2 to about 115 of SEQ ID NO:4, wherein said polypeptide has at least one conservative amino acid substitution and at least 90 % identity with SEQ ID NO:4 , as recited in claim 3; D) any composition comprising an isolated polynucleotide encoding a polypeptide comprising an amino acid sequence from 4 to 50 of SEQ ID NO: 4 or at least 90 % identical to a polypeptide comprising an amino acid sequence from 4 to 50 of SEQ ID NO:4 as recited in claim 14 encompassed by the claimed invention other than "nucleic acids set forth by SEQ ID NO: 3" or " a polynucleotide encoding a polypeptide comprising from amino acid 1 to amino acid 115 of SEQ ID NO:4, or " a polynucleotide encoding a polypeptide comprising from amino acid 2 to amino acid 115 of SEQ ID NO:4" would be expected to have greater differences in their activities. Since the amino acid sequence of a polypeptide determines its structure and functional properties, predictability of which changes can be tolerated in a polypeptide's amino acid sequence and still retain similar functionality requires knowledge of, and guidance with regard to, which amino acids in the polypeptide's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification) and detailed knowledge of the ways in which a polypeptide's structure relates to it's functional usefulness. However, the problem of predicting polypeptide structure from mere sequence data of a single amino acid sequence and in turn utilizing predicted structural determinations to ascertain binding or functional aspects of EGFH2, and finally, what changes can be tolerated with respect thereto is complex and well outside the realm of routing experimentation.

Thus, it is the Examiner position that Applicant has not provided sufficient guidance to enable one skill in the art to make claimed : A) *any* isolated nucleic acid molecule comprising a polynucleotide recited in claim 1 (d); B) *any* isolated nucleic acid molecule comprising a polynucleotide encoding a polypeptide having amino acid sequence from 1 to 115 of SEQ ID NO:4, or from about 2 to about 115 of SEQ ID NO:4, wherein said polypeptide has at least one conservative amino acid substitution and at least 90 % identity with SEQ ID NO:4 , as recited in claim 3; D) any composition comprising an isolated polynucleotide encoding a polypeptide comprising an amino acid sequence from 4 to 50 of SEQ ID NO: 4 or at least 90 % identical to a polypeptide comprising an amino acid sequence from 4 to 50 of SEQ ID NO:4 as recited in claim 14 in manner reasonably correlated with the scope of the claims. The scope of the claims

must bear a reasonable correlation with the scope of enablement. *In re Fisher*, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

In view of the quantity of experimentation necessary, the unpredictability of the art, the lack of sufficient guidance in the specification, the limited working examples, and the limited amount of direction provided given the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

The following new grounds of rejections are necessitated by amendment filed 12/01/04

4. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claim 14 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. Claim 14 (b) recited "an amino acid sequence at least 90 % identical to said amino acid sequence of (a), wherein said polypeptide is identical to amino acid 2 to amino acid 115 of SEQ ID NO:4". Claim 14(a) recited an amino acid sequence from amino acid 4 to amino acid 50 of SEQ ID NO:4, i.e. amino acid sequence of 46 amino acids. It is unclear how can amino-acid sequence of 46 amino acids be identical to an amino acid sequence of 113 amino acids ?

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1, 4-9 and 14 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. *This is a New Matter rejection*:

" A polynucleotide encoding a polypeptide having at least one specific conservative amino acid changes selected from the group recited in claims 1(d) and 14 (b) claimed in claims 1 and 14, represents a departure from the specification and claims as originally filed. The Specification and claims as originally filed only supports " a polynucleotide encoding a polypeptide having at least one conservative amino acid changes"
Applicant asserts that the specification at page 11, lines 13-17 provides a support for recited specific conservative amino acid substitution in said polypeptide.

Contrary to Applicant's assertion the specification at page 11, lines 13-17 only disclosed the general method by which Applicant calculated a sequence identity or percent conservation or which of two residues represent a conservative substitution. The specification further disclosed the examples of conservative amino acid changes that satisfied Applicant's requirement.

9. Claim 2 is allowed.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is 571/272-0840. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571/272-0841.
The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michail Belyavskyi, Ph.D.
Patent Examiner
Technology Center 1600
February 9, 2004

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600